

**AMENDMENT**

Please amend the application without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

**In the Claims**

1. (Previously presented) A method for decreasing regulatory CD4+ T cell activity comprising exposing a regulatory CD4+ T cell to a modulator of Notch intracellular domain (Notch IC) protease activity, wherein the modulator is an inhibitor of presenilin or of presenilin-dependent gamma-secretase.
2. (Cancelled)
3. (Original) The method of claim 1, wherein the presenilin is Presenilin-1 (PS1) or Presenilin-2 (PS2).
4. (Previously presented) The method of claim 1, wherein the inhibitor is selected from the group consisting of polypeptides, fragments thereof, linear peptides, cyclic peptides, nucleic acids encoding therefor, synthetic compounds, natural compounds, low molecular weight organic compounds, low molecular weight inorganic compounds and antibodies.
5. (Previously presented) The method of claim 1, further comprising exposing the regulatory CD4+ T cell to an agent that down-regulates the Notch signalling pathway.
- 6-11. (Cancelled)
12. (Withdrawn) The method of claim 1, wherein the inhibitor of presenilin is 26S proteasome or Sel 10 or a nucleic acid sequence encoding therefor.
13. (Cancelled)
14. (Withdrawn) The method of claim 5, wherein the agent that down-regulates the Notch signalling pathway is a polypeptide selected from the group consisting of a Toll-like receptor, a cytokine, a bone morphogenetic protein (BMP), a BMP receptor and an activin, or is a nucleic acid sequence encoding therefor.
15. (Cancelled)
16. (Previously presented) The method of claim 1, further comprising administering a selected antigen or antigenic determinant, or a nucleic acid encoding the antigen or antigenic determinant, simultaneously, contemporaneously, separately or sequentially with the modulator.

17. (Previously presented) The method of claim 16, wherein the antigen or antigenic determinant is a tumour antigen or antigenic determinant or an antigen or antigenic determinant of a pathogen.

18-29. (Cancelled)

30. (Previously presented) The method of claim 1, wherein the regulatory CD4+ T-cell is a Tr1 regulatory T-cell.

31-32. (Cancelled)

33. (Previously presented) The method of claim 1, wherein the regulatory CD4+ T-cell is a Th3 regulatory T-cell.

34-35. (Cancelled)

36. (Original) The method of claim 1, wherein the modulator is administered to a subject *in vivo*.

37. (Withdrawn) The method of claim 1, wherein the modulator is administered to a cell *ex vivo*.

38-41. (Cancelled)

42. (Previously presented) A method for modulating cytokine expression in regulatory CD4+ T cells comprising exposing a regulatory CD4+ T cell to a modulator of Notch intracellular domain (Notch IC) protease activity, wherein the modulator is an inhibitor of presenilin or of presenilin-dependent gamma-secretase.

43-46. (Cancelled)

47. (Previously presented) The method of claim 42, wherein the cytokine is IL-10 or IL-4, and wherein expression of the cytokine is decreased.

48. (Cancelled)

49. (Previously presented) The method of claim 47, wherein the cytokine is IL-10.

50. (Previously presented) The method of claim 47, wherein the cytokine is IL-4.

51. (Previously presented) The method of claim 42, wherein the cytokine is IL-2, IL-5, TNF-alpha, IFN-gamma or IL-13, and wherein expression of the cytokine is increased.

52. (Cancelled)

53. (Previously presented) The method of claim 51, wherein the cytokine is IL-2.

54. (Previously presented) The method of claim 51, wherein the cytokine is IL-5.

55. (Previously presented) The method of claim 51, wherein the cytokine is TNF-alpha.
56. (Previously presented) The method of claim 51, wherein the cytokine is IFN-gamma.
57. (Previously presented) The method of claim 51, wherein the cytokine is IL-13.
- 58-59. (Cancelled)
60. (Previously presented) The method of claim 42, wherein IL-10 expression is decreased and IL-5 expression is increased.
61. (Previously presented) The method of claim 42, wherein IL-10 expression is decreased and IL-2, IFN-gamma, IL-5, IL-13 and TNF-alpha expression are increased.
- 62-64. (Cancelled)
65. (Original) The method of claim 42, wherein the modulator is administered to a subject *in vivo*.
66. (Withdrawn) The method of claim 42, wherein the modulator is administered to a cell *ex vivo*.
- 67-99. (Cancelled)
100. (Previously presented) The method of claim 1, wherein the inhibitor is a small molecule inhibitor.
101. (Currently amended) The method of claim 100, wherein the inhibitor is MW167 having Formula I[[]]:

